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REMARKS

Claims 27, 38, 45, 48, 49, 50, 52, 60 and 125-130 are pending in the subject application. The Examiner has indicated that claim 126 is allowed and withdrawn claims 38, 129 and 130 from further consideration in the subject application. Applicants have hereinabove cancelled claim 125 without prejudice or disclaimer. In addition, applicants have hereinabove amended claims 27, 45, 49, 52 and 128. Support for these amendments may be found inter alia in the specification as follows: claim 27: page 41, lines 17-23; Figure 10; claim 45: page 49, lines 36-37; and page 81, lines 4-5. The remaining changes to the claims merely introduce minor grammatical and format changes. These amendments do not involve any issue of new matter. Therefore, entry of this amendment is respectfully requested such that claims 27, 45, 48, 49, 50, 52, 60 and 126-128 will be pending and under examination.

In view of the arguments set forth below, applicants maintain that the Examiner's rejections have been overcome and respectfully request that the Examiner reconsider and withdraw the various grounds of rejection.

Restriction Requirement

The Examiner stated that applicants' election with traverse of Invention II, claims 27, 48 and 125-128, in the paper filed November 17, 2003 is acknowledged. The Examiner stated that applicants' traversal is not found persuasive.

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The Examiner stated that upon examination of the MNR2 protein, the full-length MNR2 protein is allowable. Therefore, the Examiner stated that the Examiner has examined the methods of treatment utilizing the MNR2 protein, claims 45, 49, 50, 52, and 60, in accordance with *In re Ochiaie*.

The Examiner stated that the requirement is still deemed proper and is therefore made final. The Examiner stated that claims 38, 129, and 130 has been withdrawn from further consideration because these claims are drawn to non-elected inventions. The Examiner stated that claims 27, 45, 48, 49, 50, 52, 60, and 125-128 are under examination.

In response, applicants respectfully traverse. Applicants respectfully request that the Examiner reconsider and withdraw the restriction requirement such that claims 38, 129 and 130 will be examined in connection with the subject application.

Rejection Under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 27, 45, 48, 49, 50, 52, 60, 127, and 128 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regards as the invention.

Claim 27

The Examiner stated that claim 27 is not comprehensible. The Examiner stated that it is not clear what a homeobox motor neuron restricted pattern is. The Examiner stated that the

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acronym MNR2 is used, making this name unclear. The Examiner stated that MNR2 is not defined such that one skilled in the art could recognize the limitations of the claim. The Examiner directed applicants to see also the dependent claims.

In response, applicants respectfully traverse the Examiner's rejection. Nevertheless, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have hereinabove amended claim 27. Newly amended claim 27 now recites "An isolated homeobox motor neuron restricted pattern protein designated MNR2 comprising consecutive amino acids having the amino acid sequence set forth in SEQ ID NO:1" Applicants contend that this amendment obviates the above rejection of claim 27 and the claims which depend therefrom. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claim 45

The Examiner stated that in claim 45, it is not clear how only a single somatic motor neuron will be affected by the systemic administration of MNR2. Also, the Examiner questioned what the somatic motor neuron is being differentiated into.

In response, applicants respectfully traverse the Examiner's rejection. Applicants note that claim 45 does not recite a specific method of administration. Nor do applicants limit administration of MNR2 to systemic administration as the Examiner asserts. Instead, on page 53, lines 3-13 of the subject specification applicants teach that the protein may be

administered locally, i.e. intramuscularly, intrathecally, epidurally, intraperitoneally or subcutaneously, as a liquid pharmaceutical composition. Furthermore, applicants also note that the method of administering MNR2 will vary with the particular type of pharmaceutical composition comprising the MNR2 protein and can be easily determined by those of skill in the art (see page 53, line 33 - page 54, line 7 of the subject specification). One of skill in the art may easily determine the mode of administering the MNR2 protein so as to cause the differentiation of a single motor neuron.

In addition, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have hereinabove amended claim 45. Newly amended claim 45 now recites "A method of inducing differentiation of a neural progenitor cell into a somatic motor neuron in a subject comprising administering to the subject the protein of claim 27 in an amount effective to induce differentiation of the neural progenitor cell into a somatic motor neuron, so as to thereby induce differentiation of the neural progenitor cell into a somatic motor neuron in the subject."

Applicants contend that these remarks obviate the above rejection of claim 45. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

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Claims 49, 50, 52 and 60

The Examiner stated that in claim 49, it is not clear what abnormality is associated with a lack of one or more normally functioning motor neurons. Also, the Examiner stated that the phrase "effective to a generate" is awkward. The Examiner directed applicants to see also claims 50 and 52.

In response, applicants respectfully traverse the Examiner's rejection. On page 72, lines 14-16 applicants set forth that "a 'normally functioning motor neuron' is a motor neuron that can control muscle contraction and respond to sensory input." Therefore, an "abnormality associated with a lack of one or more normally functioning motor neurons" would include any abnormality wherein the motor neuron can no longer control muscle contraction or respond to sensory input normally. For example, any trauma to a motor neuron or genetic defect of a motor neuron that would cause the motor neuron to function abnormally would be encompassed by this claim. Applicants contend that whether such an abnormality exists in a subject would be easily determinable by one of skill in the art.

In addition, with respect to the allegedly awkward language of claims 49, 50 and 52, without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application, applicants have hereinabove amended these claims to remove such language.

The Examiner stated that claim 50 is indefinite because the neurodegenerative disease is not stated. The Examiner stated

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that claims 52 and 60 also lack specific diseases to be treated.

In response, applicants respectfully traverse. With respect to claim 50, applicants have set forth on page 73, lines 7-11 of the subject specification two examples of neurodegenerative diseases, e.g. spinal muscular atrophy and amyotrophic lateral sclerosis (Lou Gehrig's Disease). Therefore, one of skill in the art would know what is meant by a neurodegenerative disease. Accordingly, applicants contend that claim 50 is not indefinite to those of skill in the art.

In addition, with respect to claim 52, applicants note that what constitutes an "acute nervous system injury" is well known by those of skill in the art. For example, applicants attach hereto as **Exhibit C** an article entitled "Acute Nerve Injury" which sets forth on page 1 the various synonyms for an "acute nerve injury." Applicants also attach hereto as **Exhibit D** Notice NS-01-004 published on December 20, 2000 by the National Institute of Neurological Disorders And Stroke (NINDS) which discusses "acute spinal cord injuries". Therefore, at the time the subject application was filed the meaning of an "acute nervous system injury" was well known by those of skill in the art. Accordingly, applicants contend that claim 52 is not indefinite to those of skill in the art.

Finally, with respect to claim 60, applicants note that what constitutes a "neuromuscular disease" is well known by those of skill in the art. For example, applicants attach hereto as **Exhibit E** a copy of the webpage from The Department of

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Neurology at Baylor College of Medicine which sets forth the definition of a neuromuscular disorder/disease and a listing of specific examples (see also **Exhibit F**, copy of webpage from The Department of Neurology at Wake Forest University Baptist Medical Center). Therefore, at the time the subject application was filed the meaning of an "neuromuscular disease" was well known by those of skill in the art. Accordingly, applicants contend that claim 60 is not indefinite to those of skill in the art.

Applicants contend* that these remarks obviate the above rejections. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection Under 35 U.S.C. §112, First Paragraph

Written Description

The Examiner rejected claims 27, 127, and 128 under 25 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner stated that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner stated that the specification does not provide written description of mouse, rat, or human MNR2 protein.

In response, applicants respectfully traverse the Examiner's rejection. Nevertheless, applicants without conceding the correctness of the Examiner's position but to expedite

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prosecution of the subject application have hereinabove amended claim 128. Newly amended claim 128 no longer recites "mouse, rat or human" with respect to the MNR2 protein of claim 127. Applicants contend that this amendment obviates the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Enablement

The Examiner stated that claims 27, 45, 48, 49, 50, 52, 60, 127, and 128 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for MNR2 comprising SEQ ID NO: 1, does not reasonably provide enablement for all MNR2. The Examiner stated that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The Examiner stated that in *Ex parte Forman* (230 USPQ 546) the Board considered the issue of enablement in molecular biology. The Examiner stated that the Board held that the following factors should be considered to determine whether the claimed invention would require of the skilled artisan undue experimentation: (1) quantity of experimentation necessary: The Examiner stated that it would require undue experimentation to acquire all MNR2 across all species, to the scope of the claims; (2) amount of direction or guidance presented: The Examiner stated that at page 45 and 47+ of the specification, routineers in the field are invited to find for themselves, the scope of the MNR2 proteins as claimed, via

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nucleic acid probes, or antibody assays; (3) presence or absence of working examples: The Examiner stated that there are none; (4) the nature of the invention; (5) state of the prior art; (6) relative skill of those in the art: The Examiner stated that the invention is highly technical and the MNR2 protein is not recognized in the prior art. The Examiner stated that those working in the art are highly skilled; (7) predictability or unpredictability of the art: The Examiner stated that finding a protein that is involved in the differentiation of neurons is highly unpredictable; and (8) breadth of the claims: The Examiner stated that the claims are very broad. The Examiner stated that for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention.

In response, applicants respectfully traverse the Examiner's rejection. Nevertheless, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have hereinabove amended claim 27. Newly amended claim 27 now recites "An isolated homeobox motor neuron restricted pattern protein designated MNR2 comprising consecutive amino acids having the amino acid sequence set forth in SEQ ID NO:1 or a fragment having the biological activity thereof." Applicants contend that this amendment obviates the above rejection of claim 27 and claims 45, 48, 49, 50, 52, 60, 127, and 128 which depend therefrom. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

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The Examiner rejected claims 45, 49, 50, 52 and 60 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. The Examiner stated that the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner stated that these claims are drawn to methods of treating neurological diseases/injuries by administering the MNR2 protein systemically to a subject, thus causing differentiation of neuronal precursor cells. The Examiner stated that these methods are not art-recognized such that there could be a nexus between other prior art proteins and the treatment of neurological disease/injury and MNR2.

The Examiner stated that in *Ex parte Forman* (230 USPQ 546) the Board considered the issue of enablement in molecular biology. The Examiner stated that the Board held that the following factors should be considered to determine whether the claimed invention would require of the skilled artisan undue experimentation: (1) quantity of experimentation necessary: The Examiner stated that it would require undue experimentation to determine how one would treat diseases/injuries that are not known to be routinely treatable with a new protein that is involved with neuronal cell differentiation; (2) amount of direction or guidance presented: The Examiner stated that page 50+ provides a generic discussion of methods of treatment using protein, and these methods are not specific to neural abnormalities; (3) presence or absence of working examples: The Examiner stated

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that there are none; (4) nature of the invention; (5) state of the art; (6) relative skill of those in the art: The Examiner stated that the invention is highly technical and the MNR2 protein is not recognized in the prior art. The Examiner stated that those working in the art are highly skilled; (7) predictability or unpredictability of the art: The Examiner stated that finding a protein that is involved in the differentiation of neurons is highly unpredictable - using the protein to differentiate neuronal cells *in vivo* is highly unpredictable; and (8) breadth of the claims: The Examiner stated that the claims are very broad. The Examiner stated that for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention.

In response, applicants respectfully traverse the Examiner's rejection. Applicants note that claims 45, 49, 50, 52 and 60 do not recite a specific method of administration. Nor do applicants limit administration of MNR2 to systemic administration as the Examiner asserts. Instead, on page 53, lines 3-13 of the subject specification applicants teach that the protein may be administered locally, i.e. intramuscularly, intrathecally, epidurally, intraperitoneally or subcutaneously, as a liquid pharmaceutical composition. Furthermore, applicants also note that the method of administering MNR2 will vary with the particular type of pharmaceutical composition comprising the MNR2 protein which can be easily determined by those of skill in the art (see page 53, line 33 - page 54, line 7 of the subject specification). Applicants maintain that one of skill in the

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art may easily determine the mode of administering the MNR2 protein so as to cause the differentiation of a single motor neuron.

Applicants contend that these remarks obviate the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claim Objection

The Examiner objected to claim 125 as being dependent upon a rejected base claim. However, the Examiner stated that claim 125 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

In response, applicants respectfully traverse the Examiner's above objection. Nevertheless, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have hereinabove canceled claim 125 without prejudice or disclaimer to their right to pursue this claim in a later-filed application. Applicants contend that this amendment obviates the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.